Pleural Lung Diseases

Introduction

The pleural cavity is supposed to have a limited amount of fluid in it that allows for the lungs to expand and contract. The lining of the pleural cavity is mesothelium. The mesothelium is responsible for making the fluid that goes into the pleural cavity, and that fluid is drained by the lymphatics and blood vessels. The pleural cavity is normally at negative pressure, −5 cmH_2O. Diseases of the pleural cavity or pleurae have direct implications on the lung adjacent to them. Namely, the lungs are squishy, whereas the chest wall is not, so if anything gets into the pleural cavity, it is likely to crush the lung. Pleural diseases usually involve something getting into the pleural cavity that doesn't belong—air, blood, excess fluid. Pulmonary edema is a manifestation of parenchymal lung disease. But pulmonary edema can also coincide with pleural effusion. There is a hodgepodge of cellularly dissimilar conditions in this lesson, but they are clinically related, and by putting them together, we can facilitate clinical comprehension.

The goal is to understand the physical exam for the lung, what can go wrong with the pleural cavity, and how pulmonary edema forms through cardiogenic and noncardiogenic causes. We close by mentioning atelectasis.

Pulmonary Exam

Sound transmits well through a medium that is more solid, and poorly through a medium that is more air (you can better hear a faraway train by the vibrations through a solid rail than you can by the soundwaves carried through the air). Sound cannot transmit well through an intervening medium, so if there is a change in medium, the sound will not be felt or heard (if you're underwater, you can't hear the people on the pool deck talking about you).

The same principles apply to lung sounds. Because **sound travels best through a solid medium** and **travels poorly if it has to undergo a change in medium**, lung sounds are heard best through a more solid lung and heard poorly if they have to pass through a change in medium. A change in medium means there is something in the pleural space that shouldn't be, and the sound must travel through the lung and then through that other thing not a lung (a change in medium) to be heard. The lung isn't filled with air. The lung is alveoli filled with air. That would be a 'normal lung.' A "more solid lung" would have less air in it. It could be filled with fluid (edema), collapsed (atelectasis), or consolidated (pneumonia). A less solid lung would have more air in it than it is supposed to.

Auscultating lung sounds involves the patient generating sounds with their larynx, then the sound being transmitted through the lung parenchyma to where your stethoscope is. Lung sounds are either easily audible (called good lung sounds) or not easily audible (called poor lung sounds). Hearing things well means the tissue is either normal or more solid than normal. Hearing them poorly likely means more like air or a change in medium. **Fremitus** is the sensing of the sound vibrations generated by the larynx, using your hands to feel the vibrations. Increased vibration means more solid. Decreased vibration means less solid, or a change in medium. **Whispered pectoriloquy** and **egophony** do the same thing as fremitus but are performed differently. **Percussing** a thorax assesses for the consistency of the tissue just underneath. A dull thud means there is something more solid A resonant drum means something less solid (usually, it means air). You want to find the spot that is unlike the rest of the exam. With percussion, you aren't assessing the transmission of sound, just what the tissue under your fingers is giving you.

The lung is its own medium. Fluid is its own medium. Air is its own medium. We can use "change in the medium" and "gets more solid" to explain the lung findings for common pulmonary diseases.

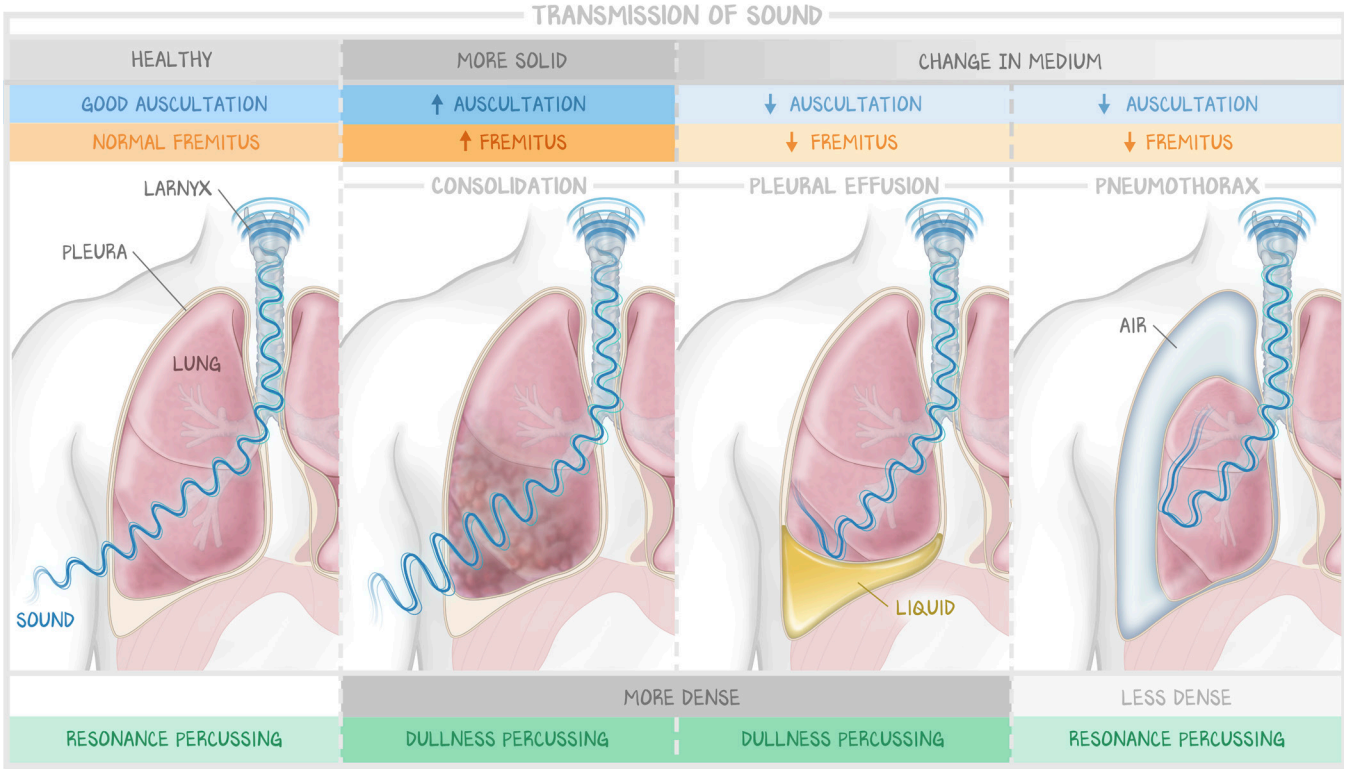


Figure 4.1: The Transmission of Sound
Lung sounds are created by air passing through the larynx. That sound originates in the larynx and is transmitted through the lung. That sound travels through the lung and arrives at the examiner's hand or stethoscope. If there is a change in medium—something other than lung is under the hand or scope—the sounds will be reduced. If there is no change in medium—lung is under the hand or scope—then the sound's transmission is dependent on the consistency of the lung. The more solid the lung, the better the sounds are transmitted. The airier the lung, the less well the sounds are transmitted. Separately, percussion adds additional clues to what might be in the chest. Something "more like air" produces tympany. Something "more solid" produces dullness.

Pneumothorax. A pneumothorax is air in the pleural space. The lung is its own medium; air is a different one. Air is "more like air" than the lung is. Because there is a change in medium, there will be reduced lung sounds and decreased fremitus. Because it is "more like air," there will be tympany rather than dullness.

Pleural effusion. A pleural effusion is fluid in the pleural space. The lung is its own medium; the effusion is a different one. The fluid is "more solid" than the lung is. Because there is a change in medium, there will be reduced lung sounds and decreased fremitus. Because it is "more solid," there will be dullness on percussion.

Consolidation. Pneumonia causes consolidation of the lung. The lung is its own medium, and the abscess is, too—the abscess is lung tissue that is "more solid" than normal. Because there is no change in medium, lung sounds are intact . . . and they will be transmitted better at the site of consolidation. Because there is no change in medium and the consolidation is more solid than the surrounding tissue, there will be an increase in fremitus. Because it is "more solid," there will be dullness on percussion.

Pulmonary edema. Fluid within the alveoli causes the sound of crackles.

Point-of-care ultrasound is replacing the need for these techniques. However, you are likely to receive a vignette that assesses your ability to interpret a pulmonary exam and give it a diagnosis.

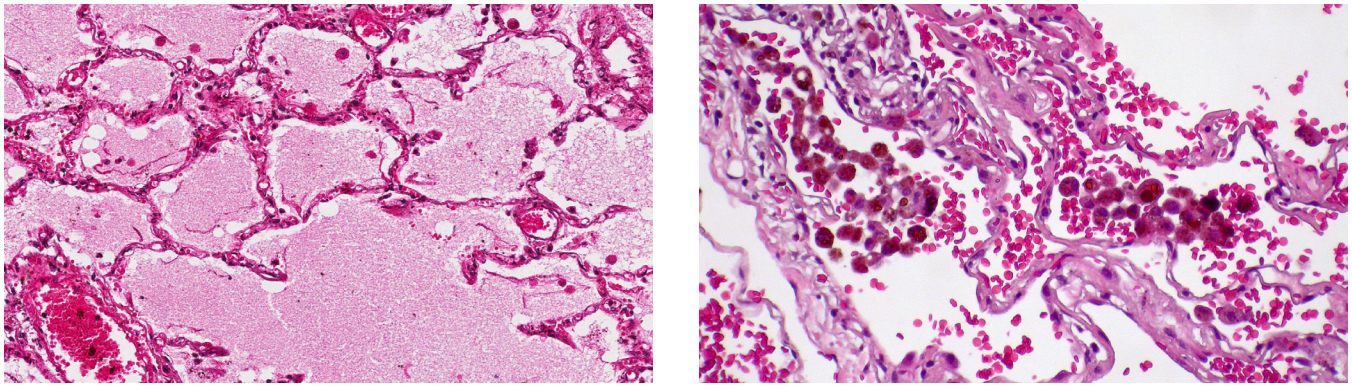
Pulmonary Edema

Pulmonary edema can be caused by either increased hydrostatic pressure or leaky capillaries. We want you seeing that there are two main causes—cardiogenic pulmonary edema (aka CHF) and acute lung injury. Although there is certainly overlap with the conditions that cause pleural effusion, those conditions are usually macroscopic in nature. We want to take this discussion of pulmonary edema to the alveoli and the alveolar septa, to monitor what's going on.

In **cardiogenic pulmonary edema**, which means left heart failure, the forward flow of blood out of the left ventricle is impaired. Therefore, fluid backs up. Fluid backs up first in the pulmonary vein, and then eventually in the pulmonary capillaries. Normal capillary function is to filter fluid on the arteriole side of the capillary and reabsorb fluid on the venule side. When the backpressure from the left ventricle reaches the capillaries, fluid cannot be reabsorbed, and so accumulates. That's the general story for hydrostatic buildup anywhere. On an X-ray, the edema will be **dependent edema,** present at the bases of the lungs. As fluid accumulates, there will be fluid **in the fissures** of the lungs.

Now let's take it to the alveolar septa.

The endothelial cells of the capillaries in the alveolar septa are tight; cells cannot get out. But during pulmonary edema, there is increased pressure. The earliest histological sign is engorged capillaries, evidenced by excess red blood cells. As the pressure continues to rise, a transudative fluid leaks out of the capillaries. "Out of the capillaries" means through the basement membrane that is shared with the type 2 pneumocytes, and that means into the alveolar spaces. What this looks like on a pathology slide is a thin pink fluid that fills the alveoli. Macrophages are responsible for monitoring the alveolar spaces as well as the blood vessels within the septa. With blood flow through the capillaries slowed, the red blood cells also slow. Macrophages do what they do whenever they sample blood and find a red blood cell that isn't efficiently passing through the vessel—phagocytosis. This leads to the engulfing and deconstruction of the red blood cells. These red blood cells have iron in them. The macrophages degrade the heme, storing the iron as hemosiderin. Hemosiderin-laden macrophages are a hallmark of congestive heart failure pulmonary edema. The fluid in the alveoli prevents their aeration (air from the airway cannot get into these alveoli), but the fluid also keeps them open (they do not collapse). Now, there are so few macrophages in the lung that this won't cause anemia or even a noticeable reduction in the red blood cell count. But histologically, you can see the macrophages on a biopsy of the lung.



(a) (b)

Figure 4.2: Histology of Pulmonary Edema
(a) The alveolar air spaces, which are supposed to be white on histology, are seen now filled with pink fluid. The walls of the alveolar septa are normal except that they are swollen with RBCs, indicative of congestion. A large blood vessel is seen in the lower left. (b) Hemosiderin-laden macrophages, even without fluid present, are indicative of CHF pulmonary edema. The macrophages are within the alveoli and stain darkly for iron.

Noncardiogenic pulmonary edema is synonymous with **acute lung injury** (ALI). Acute respiratory distress syndrome, associated with sepsis and pulmonary edema, is just one form of acute lung injury. Acute lung injury is the pathological process that accompanies pulmonary edema induced by ARDS, transfusion-related lung injury, and pancreatitis. The insult changes, but the process is consistent. When someone says "noncardiogenic," they mean "not hydrostatic," which is also synonymous with "is inflammatory." Patients will present with some precipitating event and develop **bilateral whiteout** on an X-ray.

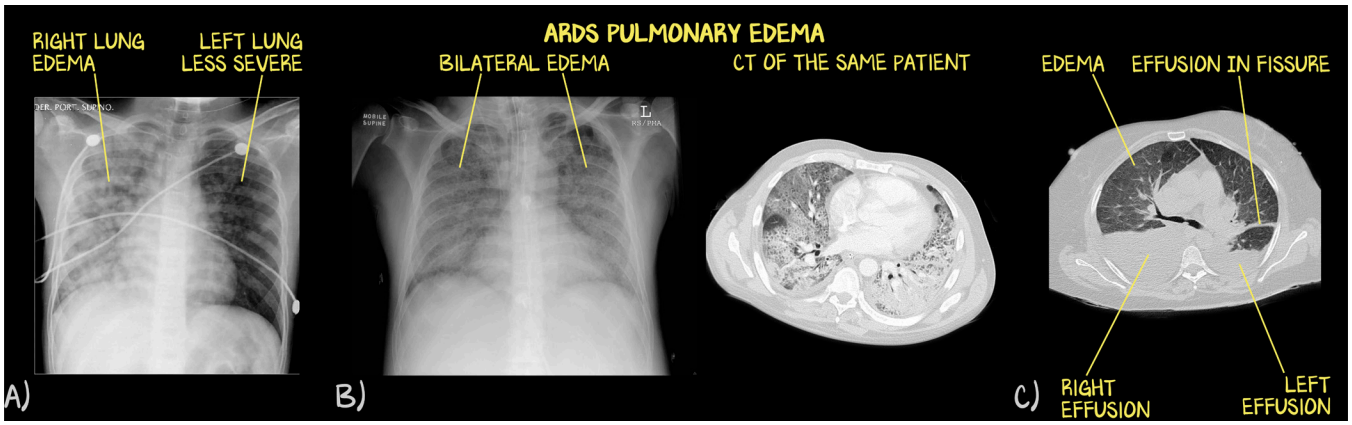


Figure 4.3: Pulmonary Edema
(a) Pulmonary edema secondary to altitude sickness. Notice how the right lung is much "fluffier" than the left. The costophrenic margins are clear, indicating that there is no effusion. (b) X-ray (left) showing bilateral opacification of the lung fields. The ribs are still visible, indicating it is not an effusion but rather interstitial edema. The CT from the same patient (right) demonstrates numerous air spaces (black, interspersed between chains of bright white, indicative that fluid is in between the alveoli within the interstitium). (c) A non-lung axial view of a patient in congestive heart failure exacerbation. The right lung has a large effusion—no air spaces are seen within it. Another sign of extrapulmonary fluid accumulation is the effusion in the fissure on the left. The pathogenesis of the effusions, which are excess fluid in the pleural cavity, and the edema seen in the anterior lungs is the same as in heart failure—backpressure forcing fluid out of capillaries. But edema is fluid leaking out of capillaries into the interstitium and then the air spaces of the alveoli, whereas an effusion is fluid leaking into the pleural cavity.

Inflammation is the key. Either pneumocytes are injured and the alveolar macrophages sense it or circulating immune mediators (as in sepsis) activate endothelial cells. The mechanisms of activation are not well elucidated, but what happens after is. **Endothelial cell activation** permits neutrophils to make it to the edge of the wall and wiggle their way out into the alveolar interstitium. **Neutrophils** enter the alveolus and the interstitium, and do what they do—gobble pathogen, call for help, die in place. Only there isn't any pathogen. More endothelial damage brings more leukocytes. More leukocytes mean more cytokines. This feedforwards the underlying pathogenesis.

The widening of the endothelium to allow neutrophils out also allows fluid and proteins out. The fluid that leaks into the alveoli is therefore exudative and fills the alveoli. The interstitium widens as leukocytes fill the space. The formation of **hyaline membranes** heralds the histologic diagnosis of **diffuse alveolar damage (DAD).** Diffuse alveolar damage can be divided into three phases—acute, organizing, and late. The acute phase is characterized by distinctive hyaline membranes lining the alveolar spaces. Endothelial cells and pneumocytes undergo necrosis. The hyaline membranes begin to organize as DAD continues into the organizing phase, and fibroblasts enter, proliferate, and lay down granulation tissue in the alveolar spaces. Type 2 pneumocytes demonstrate marked reactivity and become hyperplastic near the end of the early phase. As the organizing phase progresses, granulation tissue is incorporated into the alveolar septa, leading to organizing fibrosis. In the late phase, there is either resolution (macrophages clear the collagen and fibroblasts) or fibrosis (the dense collagen fibrosis and hyalinization of the alveolar walls become permanent). For patients who survive ARDS, many cases resolve with minimal lung damage; however, patients may develop varying degrees of end-stage lung disease.

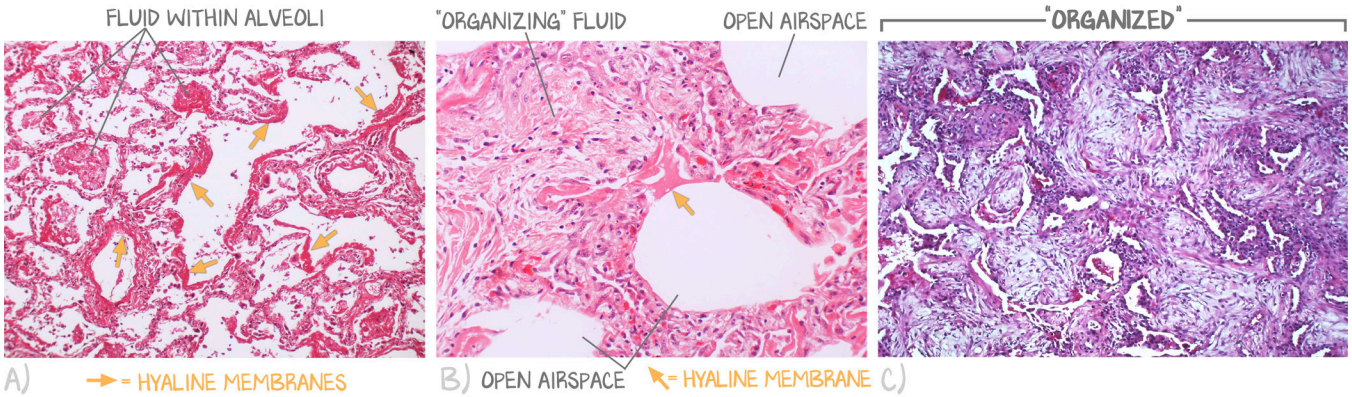


Figure 4.4: Histology of Diffuse Alveolar Damage
(a) Acute diffuse alveolar damage demonstrating hyaline membranes with little involvement of the alveolar septa. (b) The organizing phase of diffuse alveolar damage. The alveolar walls are markedly expanded by extensive fibroblast proliferation and collagen deposition. Remnants of a hyaline membrane are seen in the center. (c) In the late proliferative/organizing phase of DAD, there is extensive interstitial and intra-alveolar fibroblastic proliferation with a myxoid extracellular matrix.

The thing is, pulmonary edema is usually a clinical diagnosis and not a histological one. We used to use a right heart catheter to monitor pulmonary capillary wedge pressure. Cardiogenic pulmonary edema would cause elevated capillary wedge pressure, a surrogate for high pressures in the left ventricle. Low capillary pulmonary wedge pressure means the edema was not hydrostatic in nature and was likely to be acute lung injury.

Now, we simply use the clinical context. The person with severe pancreatitis or septic shock, or who has had a transfusion reaction, who is also hypotensive with a good ejection fraction and a brain natriuretic peptide of 4, probably has ALI. The person with an ejection fraction of 5% after their myocardial infarction, with peripheral edema, jugular venous distention, and a BNP of 5,000, probably has a cardiogenic cause.

Pleural Fluid Diseases

Pleural fluid originates from the vasculature of the parietal pleura surfaces and is absorbed by lymphatics in the dependent diaphragmatic and mediastinal surfaces of the parietal pleura. Hydrostatic pressure from the systemic vessels that supply the parietal pleura is thought to drive interstitial fluid into the pleural space. Hydrostatic forces mean no protein, and therefore the pleural fluid should have a lower protein content than the serum. The accumulation of excess fluid can occur if there is excess production, decreased reabsorption, or both overwhelming the normal homeostatic mechanism. Pleural effusions, except those known to be caused by congestive heart failure, require **thoracentesis** and fluid analysis. That is more clinical material, so we'll stay focused on the mechanisms of their creation in this lesson. You will eventually need to commit Light's criteria to memory, but not yet. Lots of proteins or lots of cells means exudate. Just a bunch of fluid means transudate.

Pleural effusions can be transudative or exudative. A **transudative effusion** is caused by **fluid and not cells** entering the pleural cavity. A transudative effusion is associated with **filtration forces**—either increased capillary hydrostatic pressure or decreased capillary oncotic pressure. An **exudative effusion** is caused by **fluid and cells** entering the pleural cavity. An exudative effusion is most often associated with **inflammation**—malignancy or infection. Because pleural fluid obeys gravity, a simple effusion will demonstrate a **horizontal meniscus** on an X-ray and will layer out when gravity is shifted. A **loculated pleural effusion** is one that does not layer out and may have a complex X-ray finding.

Transudative effusion, hydrothorax, is caused either by increased capillary hydrostatic forces or decreased capillary oncotic forces. **Volume overload** occurs in congestive heart failure exacerbation and chronic kidney disease. **Loss of oncotic pressure** can be seen in cirrhosis (makes albumin), nephrosis (protein is lost in nephrotic syndrome), and gastrosis (malnourishment/calorie deficit prevents the liver from making protein).

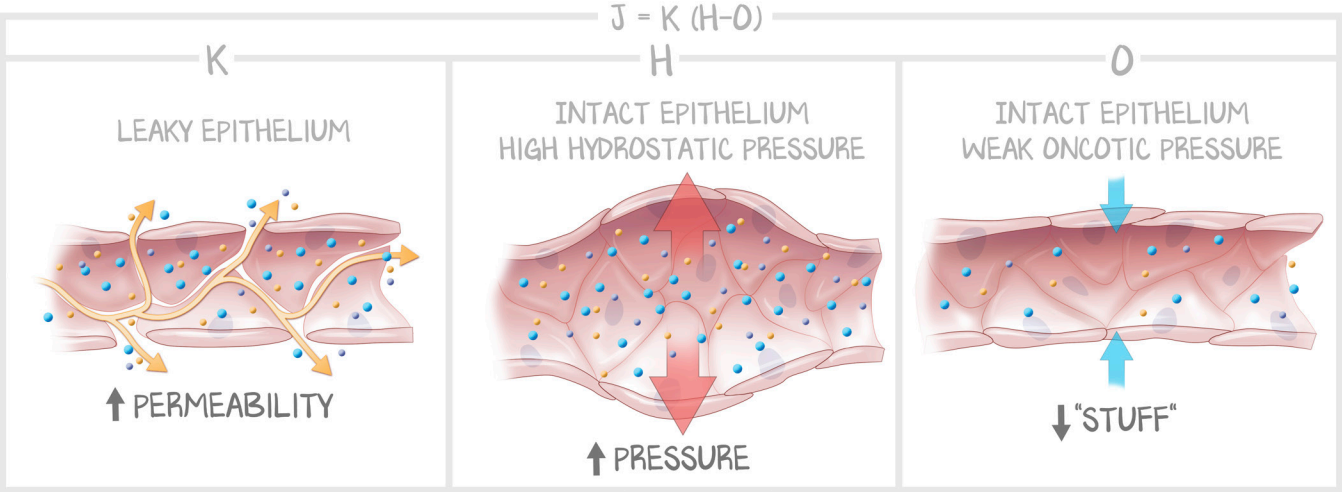


Figure 4.5: Mechanisms of Effusions
Identical to fluid where fluid shouldn't be in Cardiology, the causes of excess fluid come down to leaky epithelia, elevated hydrostatic pressure, or a loss of oncotic force. Transudates are caused by changes in the force of filtration—increases in capillary hydrostatic pressure or decreases in capillary oncotic pressure. Exudates are caused by increased permeability, allowing entire cells (along with the fluid, ions, and protein) out of the blood vessel.

A purulent effusion is called **empyema**. Technically, a parapneumonic effusion is any pleural effusion secondary to pneumonia, empyema is pus in the effusion. You should see them as more or less synonyms. Most commonly, a pulmonary infection seeds the cavity. This causes inflammation within the cavity. With the arrival of neutrophils, there will be frank pus. The fluid is often loculated, and a rind forms on the surface of the lung, which must be surgically removed. Assessment of the pleural fluid will show an exudative fluid.

Other fluids can get into the pleural space. They have specific names—chylothorax and hemothorax.

Chylothorax is an accumulation of **lymphatic fluid**. Lymphatic fluid, chyle, is milky white and contains finely emulsified fats. Lymphatics drain the pleural cavities. If the lymphatics become obstructed, the fluid backs up into the pleural cavity. Lymphatic obstruction is often caused by a malignancy in the thorax, obstructing distal lymphatics.

The escape of blood into the pleural cavity is called **hemothorax**. It is caused by trauma. Penetrating wounds lacerate an artery, or blunt trauma breaks a rib that subsequently lacerates a vessel. Hemothorax is treated with a chest tube (thoracostomy) placement, and the hemorrhage volume is assessed. Brisk or ongoing bleeding necessitates exploration (thoracotomy). Self-resolving bleeding does not.

Pleural Air Diseases

Pneumothorax. A pneumo- (air) thorax (in the thorax) is the pathologic state of air within the pleural cavity. Air can get into the pleural cavity from one of two places—either from the alveoli through the visceral pleural layer or from the atmosphere through the chest wall and the parietal layer. We also want you to think about pneumothorax with an intent to treat the pneumothorax. To be specific about

it, we use the term *simple pneumothorax* to convey "not tension pneumothorax," and modify the simple pneumothorax as either small or large. **Penetrating injuries** allow air into the chest. The pleural cavity is a relative vacuum, the intrapleural pressure around –5 cmH_2O, less than atmospheric pressure. When opened to the atmosphere, air will rush into the pleural space. With most penetrating injuries, the chest wall closes off the entrance to air, so a pneumothorax doesn't occur. There may be some air in the space, but it is negligible and needs no intervention. **Blunt trauma** can also cause a pneumothorax. A closed rib fracture can lacerate the lung, opening a connection between the alveoli and the pleural cavity. The alveoli at rest are at atmospheric pressure. When the patient inhales, the diaphragm tugs on the alveoli and the pleural cavity alike. The intrapleural pressure decreases with the alveolar pressure. Air rushes into the alveoli. Only now, with an opening into the pleural space and the pleural pressure lower than the alveolar pressure, more air enters the pleural space. On exhalation, the connection between the alveoli and the pleural space allows the air to exit through the airway. **Rupture of blebs** is how a spontaneous pneumothorax occurs, also creating a connection from the alveoli to the pleural cavity (tall, lanky men have the highest risk). In the three situations explained above, inhalation brings air into the pleural space and exhalation allows it to leave. Air in and air out is termed a **simple pneumothorax**. The air takes up space, so it will compress the lung on the affected side. A simple pneumothorax causes mild compression atelectasis. Sometimes a chest tube is required to drain the air, and sometimes the air will be absorbed by the body without intervention. The size of the pneumothorax dictates surgical intervention versus watchful waiting. A small pneumothorax may be absorbed by the body. Adding **supplemental oxygen** dilutes the nitrogen being inhaled, making it easier for the lungs to absorb the pneumothorax. Larger ones that are hemodynamically stable get a **chest tube and water seal**.

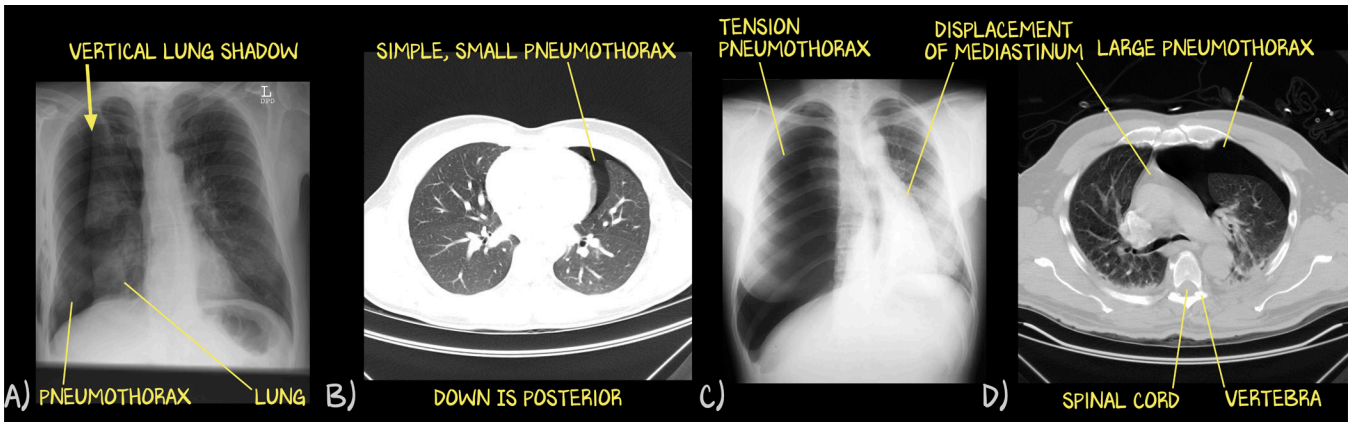


Figure 4.6: Pneumothorax
(a) A large simple pneumothorax showing the classic vertical lung line. There is air on the patient's right (left of the image). To the right of the line (medially), there is lung. There is no tracheal deviation or midline shift. (b) Axial CT with a lung window showing air rising. The patient is on their back, the heart up, and because air rises, a small simple pneumothorax rises to the top of the patient, which is the anterior chest when supine. (c) X-ray showing a tension pneumothorax with displacement of the carina and midline structures, including the heart, to the left (right of the image). Although tension pneumothorax cannot be diagnosed on imaging alone, this is certainly a serious warning sign. (d) A CT scan of a different patient who also has a large pneumothorax with mediastinal displacement. This patient has a left-sided pneumothorax (right of image), displacing the mediastinum to the right (left of image).

Tension pneumothorax. In the previous discussion of simple pneumothorax, we saw the ability to bring air into the pleural cavity with inhalation, but also get air out of the pleural cavity on exhalation. There was compression of the lung, but not a significant compromise of other structures. In a tension pneumothorax, there is a one-way valve. **Air can get into the cavity, but not out.** With each successive breath, more air fills the pleural cavity. As more and more air accumulates, more and more pressure accumulates in the pleural cavity. Just as with the simple pneumothorax, the expanding pneumothorax pushes against the chest wall (which does not budge) and against the lung (which collapses). Eventually, the lung will be

completely collapsed. The other structures in the thorax then feel the increased pressure instead. In a tension pneumothorax, the **trachea is deviated away from the affected side**, pushed by the expanding air. In a tension pneumothorax, **hypotension develops from the compression of the vena cava**. The low-pressure vessel cannot withstand the pressure from the pneumothorax. With the compromised venous return, there is no blood to be pumped out, and cardiac output is compromised. This backup of returning blood is visualized by **jugular venous distension**. A tension pneumothorax is a medical emergency and requires **needle decompression** and a subsequent chest tube (thoracostomy). Because air rises, needle decompression can be done with an IV needle, 18G or larger, at the second intercostal space.

Atelectasis

Atelectasis is the partial collapse of a lung. The alveolar air spaces are not filled with fluid, and they are not fully collapsed, either. But they show less aeration and demonstrate a higher resistance to opening.

In **resorption** atelectasis, there is a complete obstruction of a segment of the airway. Over time, air is resorbed from the dependent alveoli, which collapse. Since lung volume is reduced, the mediastinum will shift toward the atelectatic lung.

In **passive** atelectasis, the lung is compressed by an external force. This is what causes lung collapse in tension pneumothorax. Passive atelectasis is synonymous with compression or collapse caused by another thing impinging on the lung. If the mediastinum moves, it is because of the thing compressing the lung, as we saw in tension pneumothorax.

In **contraction** atelectasis, the alveoli cannot expand or are missing. For example, a fibrotic lung will not be able to inflate and deflate as well as a normal one can. The mediastinum does not move. Look for lung resection or fibrotic lung disease.

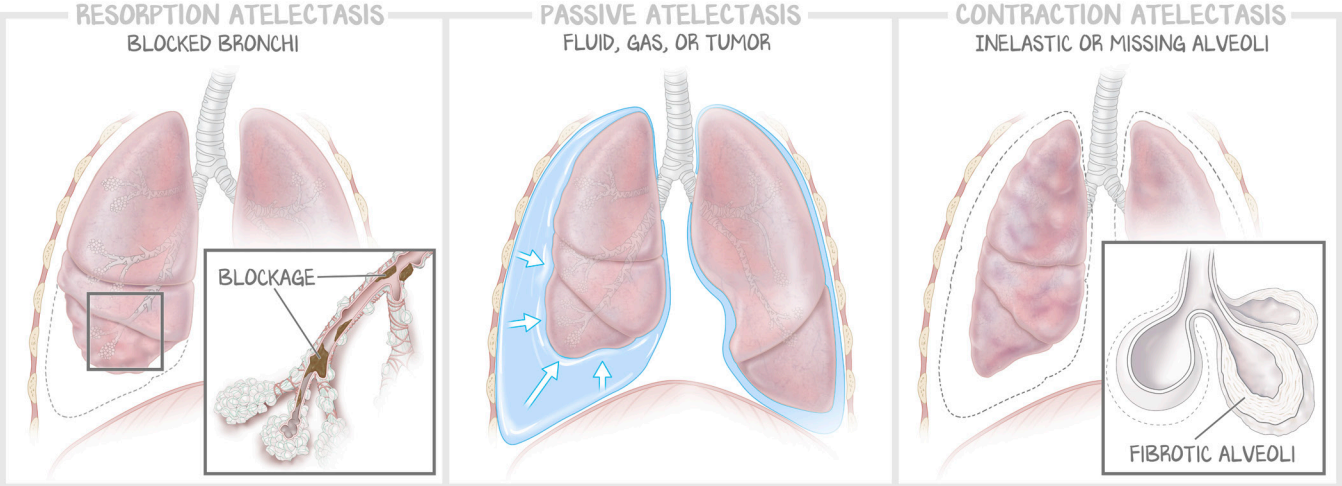


Figure 4.7: Atelectasis
A visual representation of the three categories of atelectasis.

Citations

Figure 4.2a: Originating from the University of Alabama at Birmingham, Department of Pathology PEIR Digital Library at http://peir.net pursuant to a license grant by the UAB Research Foundation.

Figure 4.2b, 4.4a, 4.4b, 4.4c: Courtesy of Yale Rosen, MD.